

REMARKS

Claims 1-5, 7, 12-19, 21 and 26-28 are pending in the instant application. Claims 7 and 21 have been rewritten as independent claims containing all of the limitations set forth in their respective base claims (*i.e.*, claim 1 and claim 15). No further claim amendments have been presented herein. Accordingly, no new matter has been added by these amendments.

Applicants note with appreciation the Examiner's withdrawal of the objections with regard to the oath/declaration and the nucleotide and/or amino acid sequence disclosure in the instant application in the previous Office Action mailed July 30, 2003. Applicants also thank the Examiner for withdrawing the rejections under 35 U.S.C. § 112, first and second paragraphs.

I. Information Disclosure Statement

Applicants thank the Examiner for her acknowledgement of the Supplemental Information Disclosure Statement filed on September 30, 2003. With regard to reference C57, the International Search Report for PCT/US02/25319, Applicants note that all category X and Y references listed on the International Search Report were individually cited in the SIDS filed on September 30, 2003. A copy of the ISR was provided solely for the Examiner's convenience.

II. Specification

The Examiner has objected to the informalities in the specification. In particular, the Examiner has objected to the recitation of "Fig. 3a" in the amendment to the specification filed December 30, 2003.

The specification has been amended herein to replace all references to "Fig. 3a" with "Fig. 3". Accordingly, Applicants request the withdrawal of this objection.

III. Claim Rejections Under 35 § 103

Claims 1-5, 12-19 and 26-28 have been rejected as being unpatentable over Soukup *et al.*, Proc. Natl. Acad. Sci. USA, vol. 96: 2484-89 (1999) ("Soukup") or Robertson *et al.*, Nucleic Acids Res., vol. 28:1751-59 (2001) ("Robertson"). According to the Examiner, "it would have

been *prima facie* obvious ... to substitute the hammerhead ribozyme and anti-theophylline aptamer as taught by Soukup *et al.* or the ligase ribozyme and anti-theophylline aptamer as taught by Robertson *et al.* with the Group I intron and aptamer of Applicant's invention," because "one of ordinary skill in the art would recognize that the hammerhead ribozyme (as taught by Soukup *et al.*), the ligase ribozyme (as taught by Robertson *et al.*), or the Group I intron ribozyme are functionally equivalent." (Office Action, page 6).

Applicants traverse the Examiner's characterization that the hammerhead ribozyme, the ligase ribozyme and the Group I intron ribozyme are functionally equivalent. In the Office Action at page 6, the Examiner has simply concluded that "all ribozymes function similarly" and are, therefore, "art-recognized functional equivalents" without presenting or citing any documentary evidence to support this assertion. In accordance with MPEP § 2144.04, Applicants request that the Examiner provide adequate evidence to support this conclusion.

In addition, Applicants submit that the Examiner has failed to establish a *prima facie* case of obviousness with regard to the Soukup and/or Robertson references. A *prima facie* case of obviousness requires some suggestion or motivation, either in the references themselves or in the knowledge generally available in the art, to modify the reference or to combine reference teachings. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). See also MPEP 706.02(j).

In the oligonucleotides of the claimed invention, the Group I intron oligonucleotide is part of a larger oligonucleotide, *i.e.*, it is coupled to an aptamer oligonucleotide to form an aptazyme. There is no teaching or suggestion in either the Soukup or Robertson reference that the hammerhead ribozyme or the ligase ribozyme, when coupled to an aptamer oligonucleotide, will have the same functionality as an aptazyme that contains a Group I intron oligonucleotide. In particular, there is nothing in the teachings of either reference that suggests that each of these different ribozymes are functionally equivalent and will be equally responsive to allosteric control when the coupled aptamer oligonucleotide interacts with its target ligand. In fact, the Robertson reference teaches away from the ribozymes being functionally equivalent -- this reference specifically chose to use the smaller ligase ribozyme to study allosteric regulation *via*

ligand-induced conformational changes in ribozyme oligonucleotides rather than a “larger, more structurally robust” ribozyme such as the Group I intron ribozyme. (See Robertson, p. 1751). There is no teaching or suggestion in the Soukup or Robertson references that a larger aptazyme, such as the Group I intron aptazymes of the claimed invention, will experience the same level of allosteric regulation, as a smaller, less structurally stable ribozyme, *e.g.*, the hammerhead and ligase ribozymes. Thus, the teachings of these references fail to provide a skilled artisan with a reasonable expectation that a larger, more structurally stable ribozyme, such as the Group I intron, can be successfully subjected to allosteric regulation when coupled to an aptamer sequence.

The fact that references can be modified does not render the resulting combination obvious unless the prior art also suggests the desirability of the combination. (See MPEP §2143.01, citing *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990)). In moving from the prior art to the claimed invention, one cannot base a determination of obviousness on what the skilled artisan might try or find obvious to *try*. Rather, the proper test requires determining what the prior art would have led the skilled artisan to *do*. As described above, there is no suggestion in either Soukup or Robertson references that would motivate a skilled artisan to modify the oligonucleotides described therein. Thus, the mere fact that the Soukup and Robertson references can be modified is not sufficient to establish a *prima facie* case of obviousness.

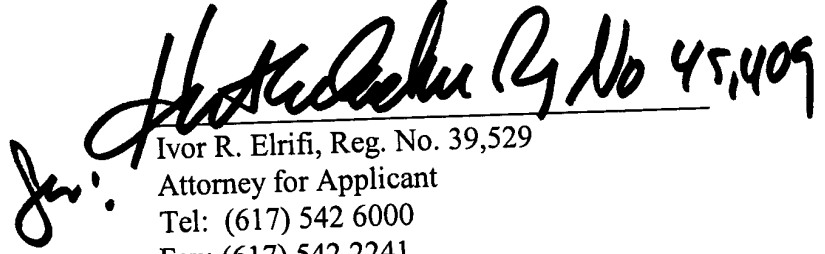
Accordingly, Applicants request that the Examiner withdraw this rejection.

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CONCLUSION

On the basis of the foregoing amendments, Applicants respectfully submit that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

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